

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

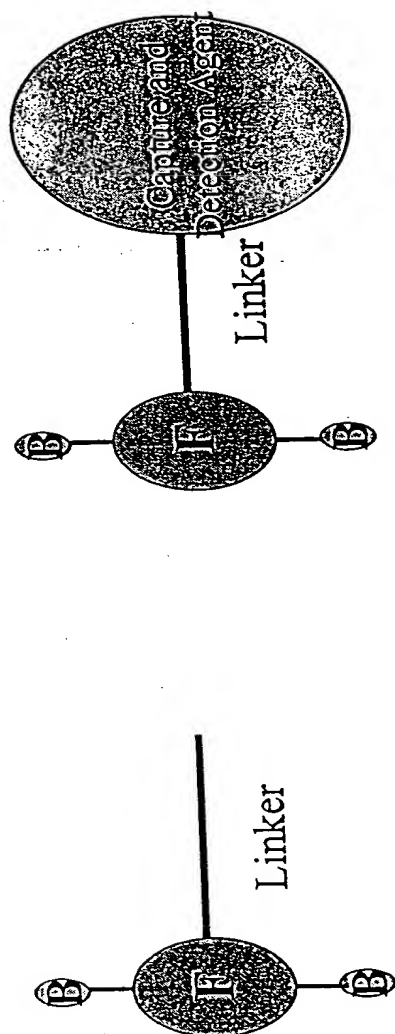
Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

High-throughput Target ID



Library of Target ID Compounds

Library of Bioactive Compounds

Use corresponding activity-based probe to identify the biological target

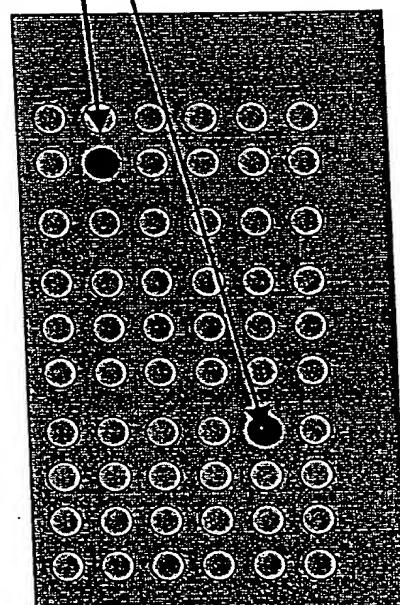
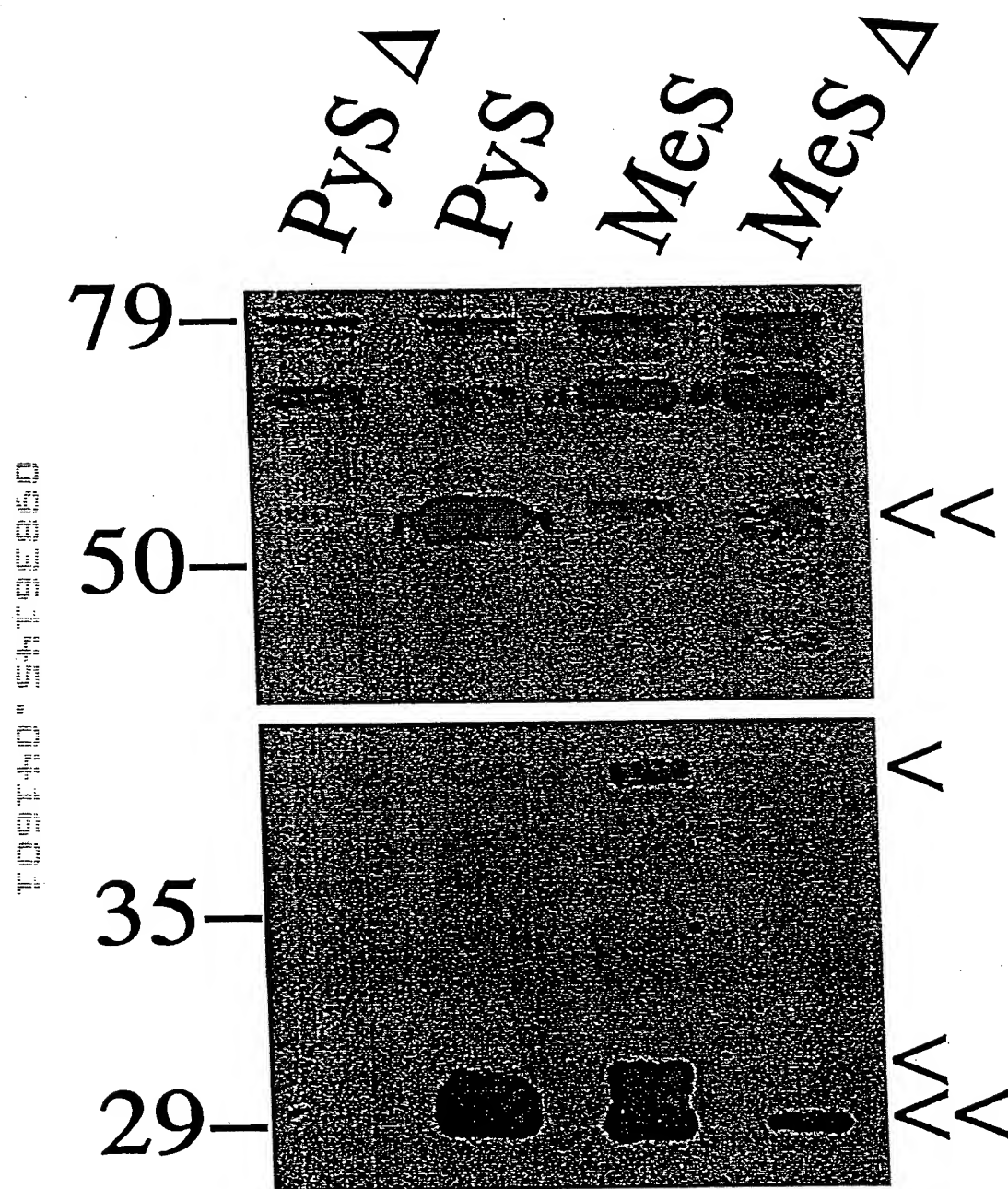


FIGURE 1



Non-Directed Tagged Library of Sulfonates Identifies Probe for ADH Superfamily of Enzymes

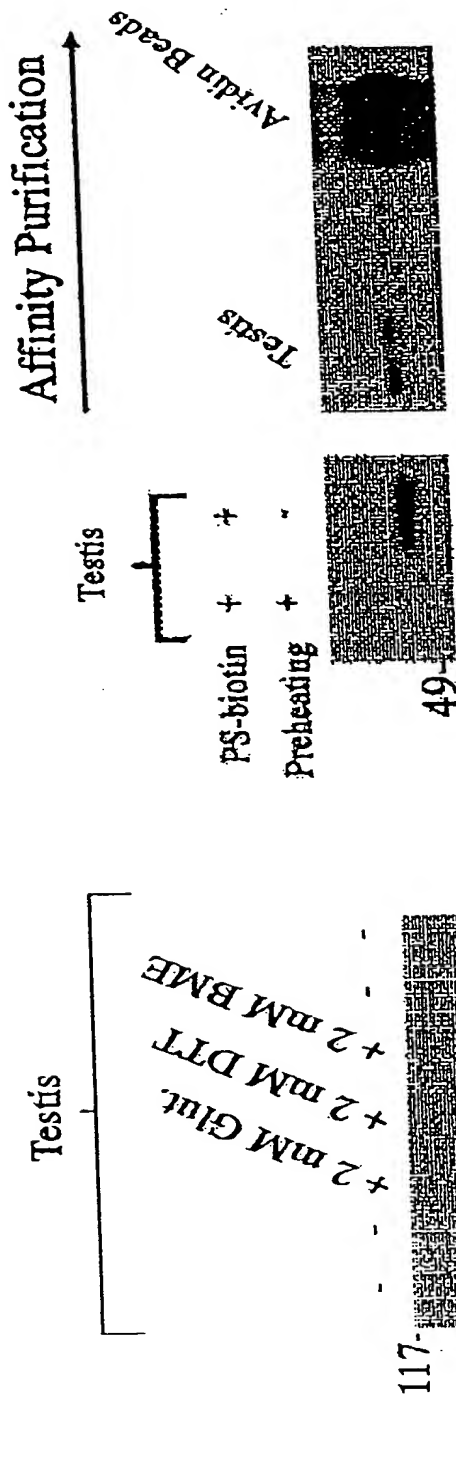
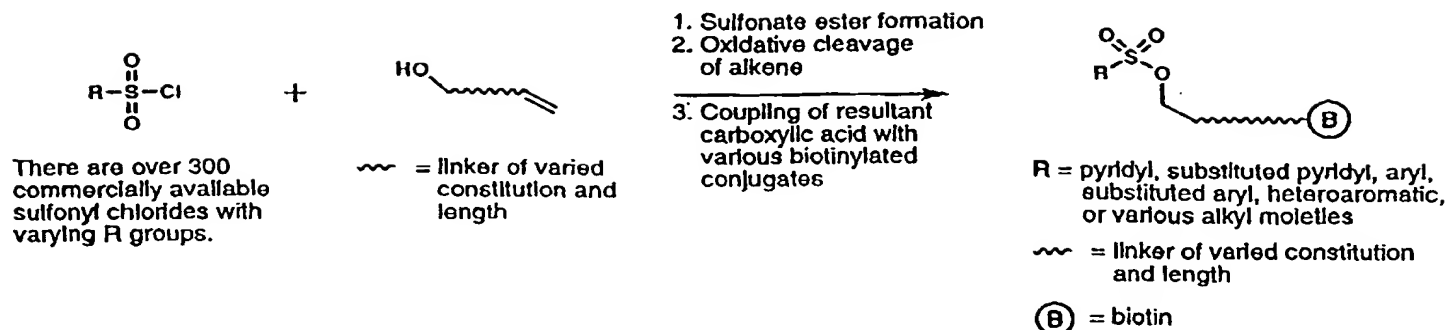


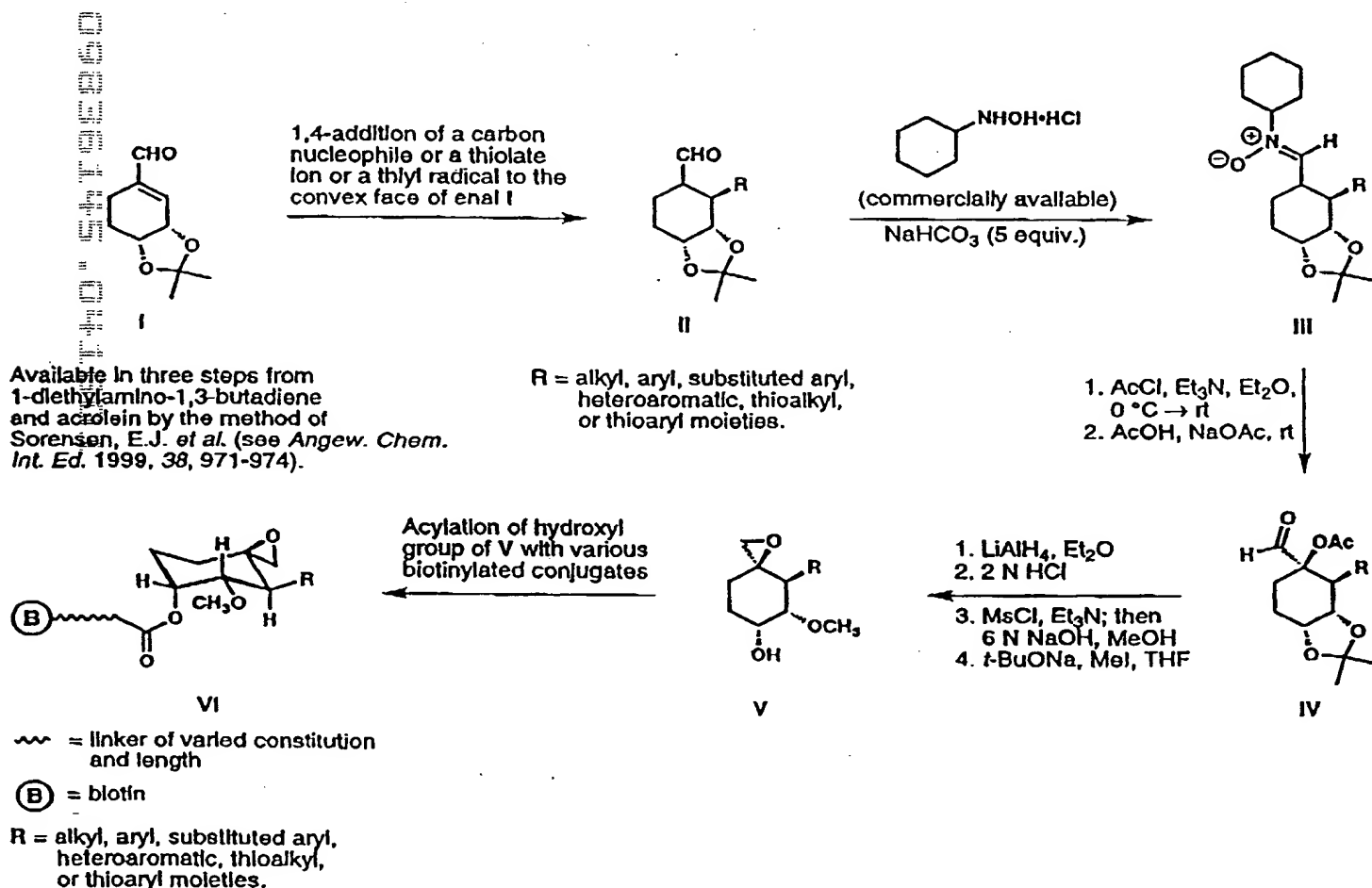
FIGURE 3

- MALDI mapping identifies tagged protein as aldehyde dehydrogenase (ADH, cytosolic class II)
- 28 ADHs in fly genome
 - Involved in retinoic acid biosynthesis and catabolism of alcohol and chemotherapeutic agents

FIGURE 4



Scheme 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for I \rightarrow II \rightarrow III \rightarrow IV \rightarrow V can be found in Sorensen, E.J. *et al.* *Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the metalloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

FP-Biotin: a kinetic reporter of SH Activity

The rates at which the majority of SHs react with FP-biotin can be experimentally followed

FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes

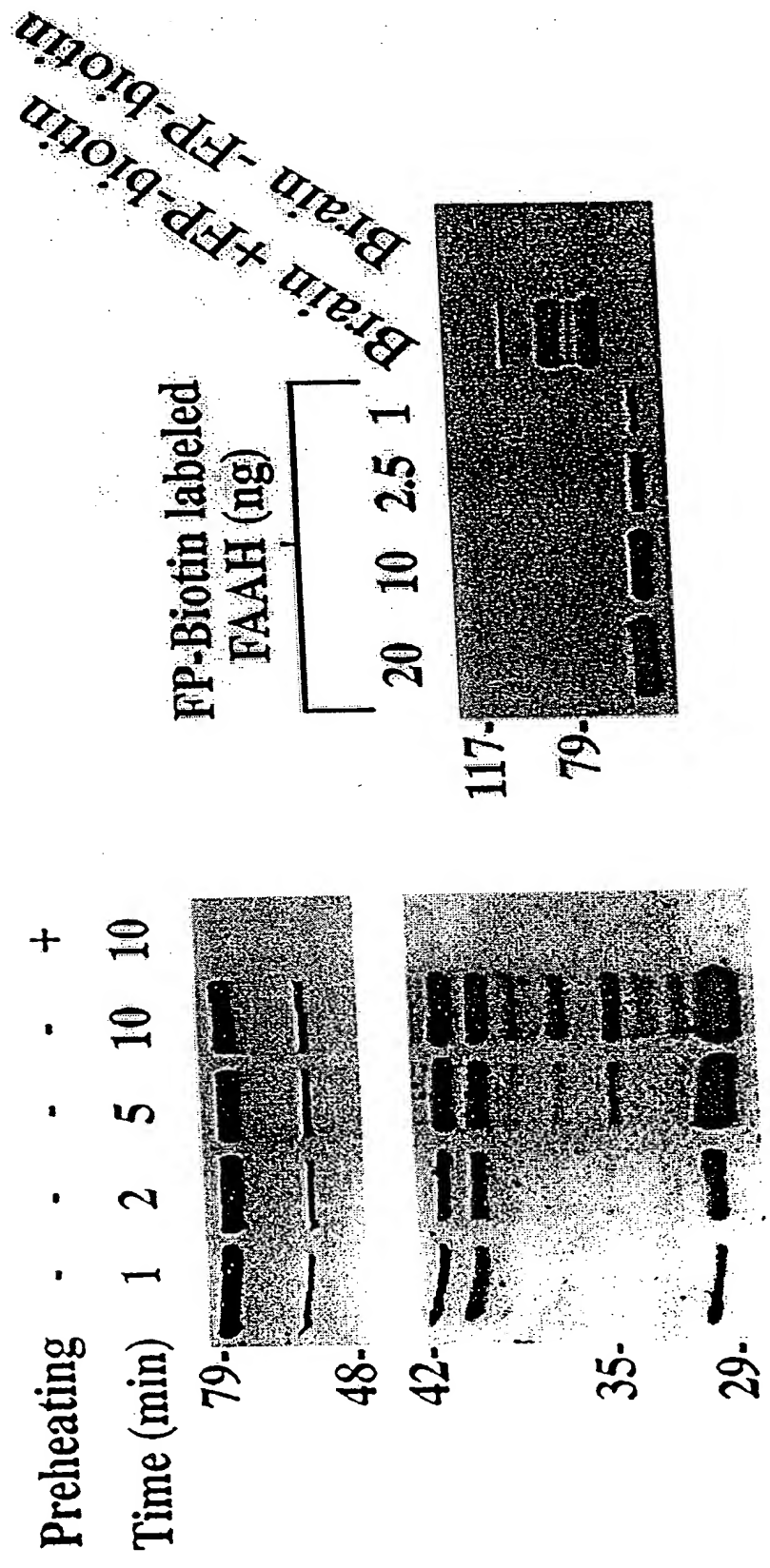


FIGURE 5

Utility of Multiplexed probes in identifying Serine Hydrolases

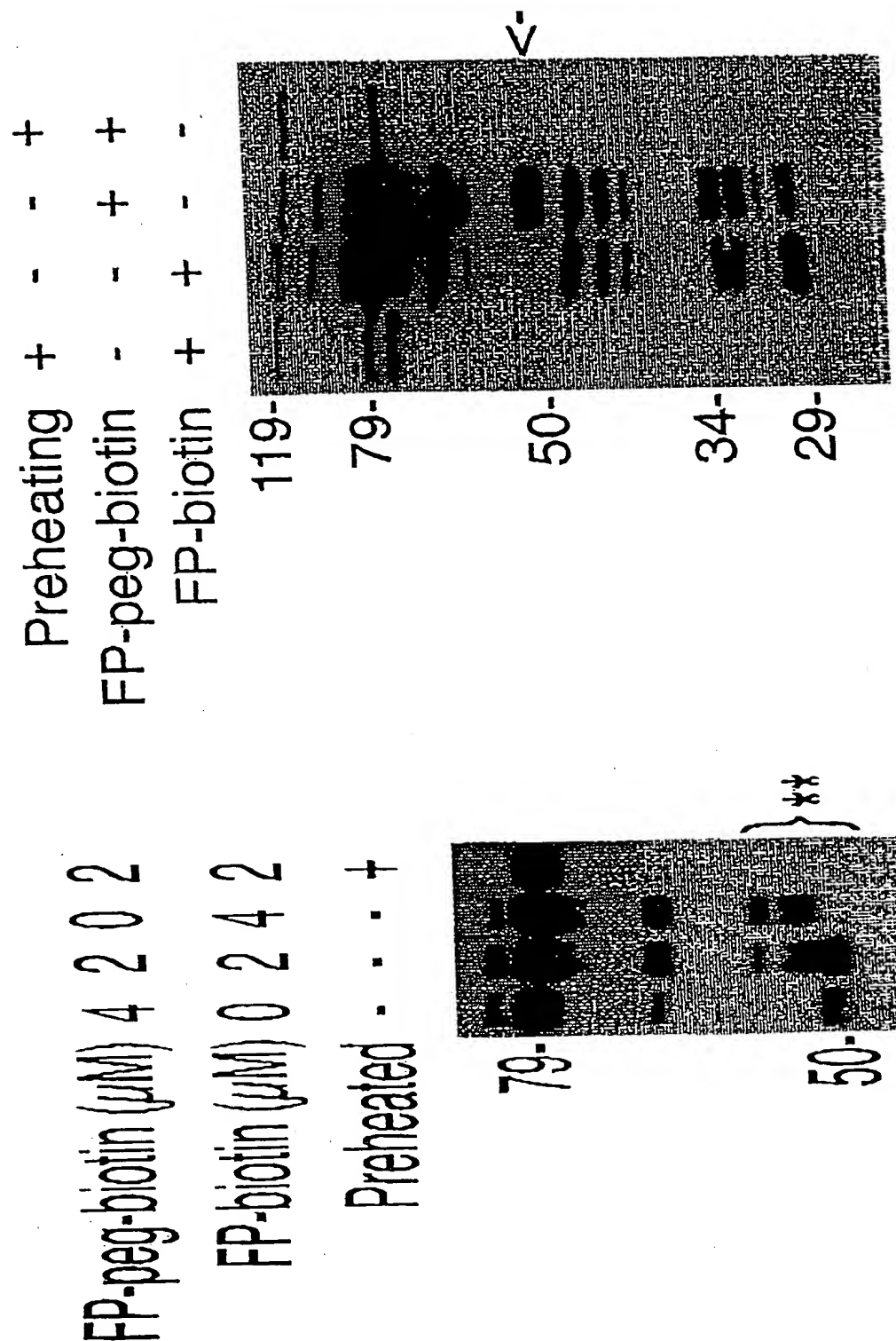


FIGURE 6

FIGURE 7

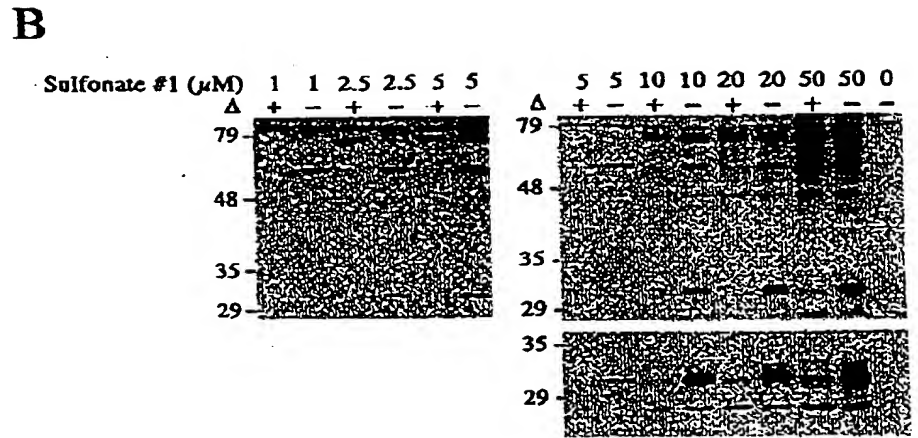
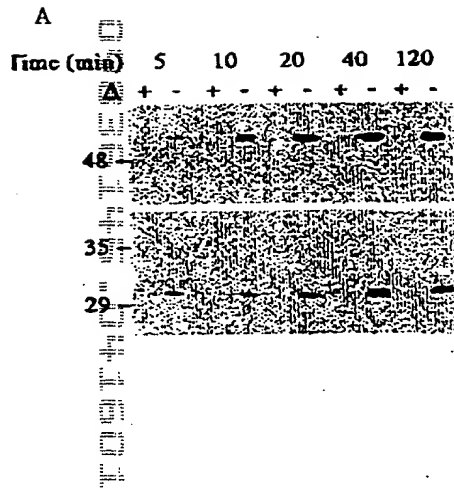
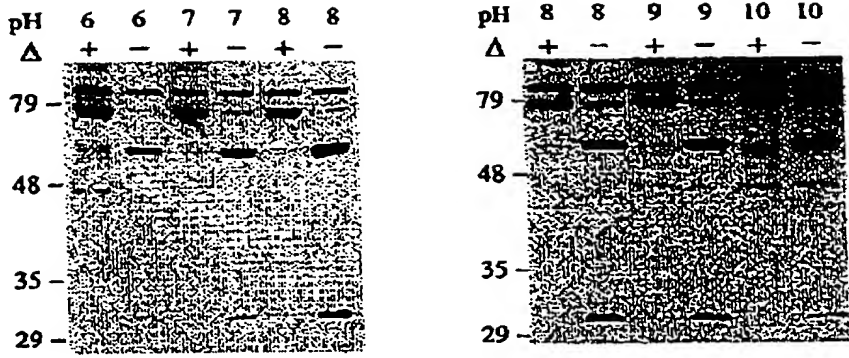


FIGURE 7

C



D

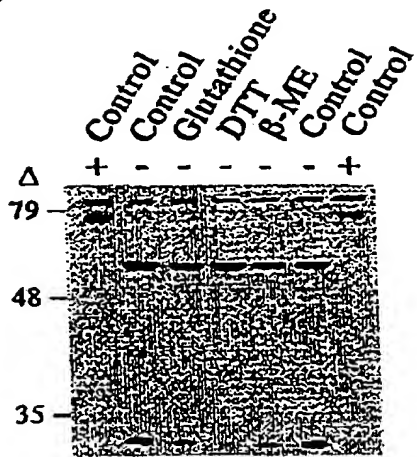


FIGURE 8

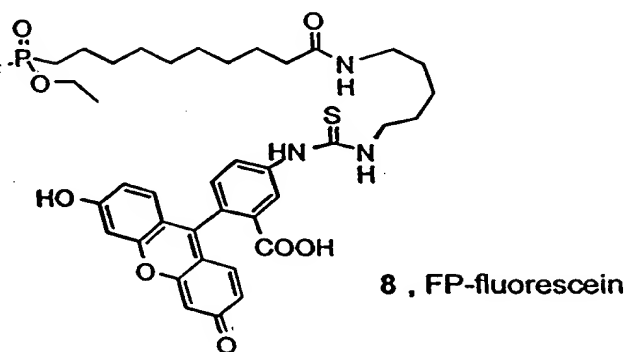
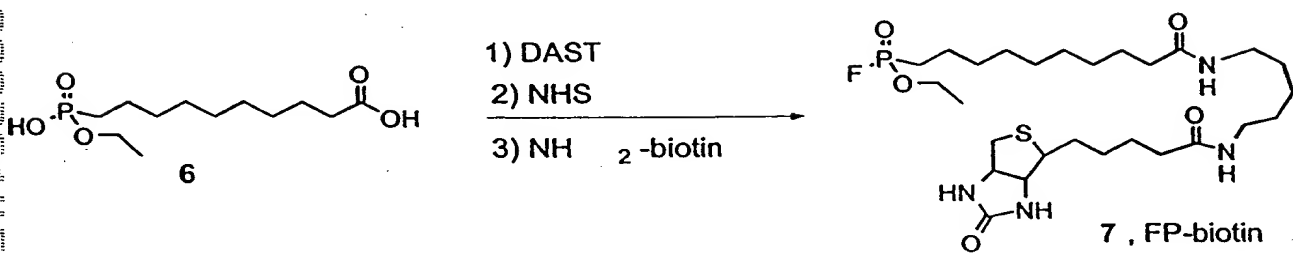
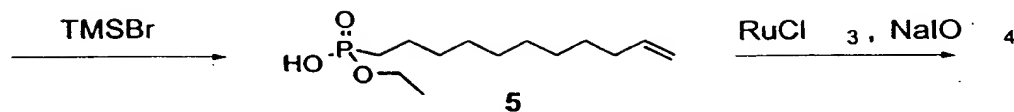
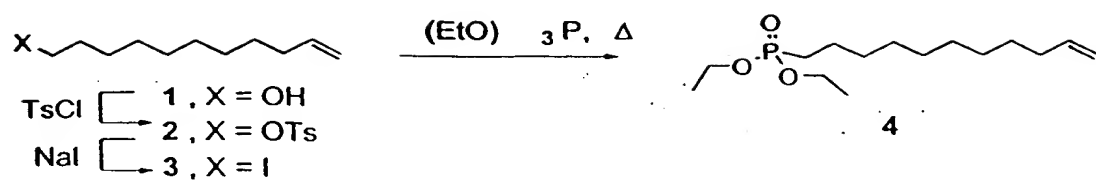
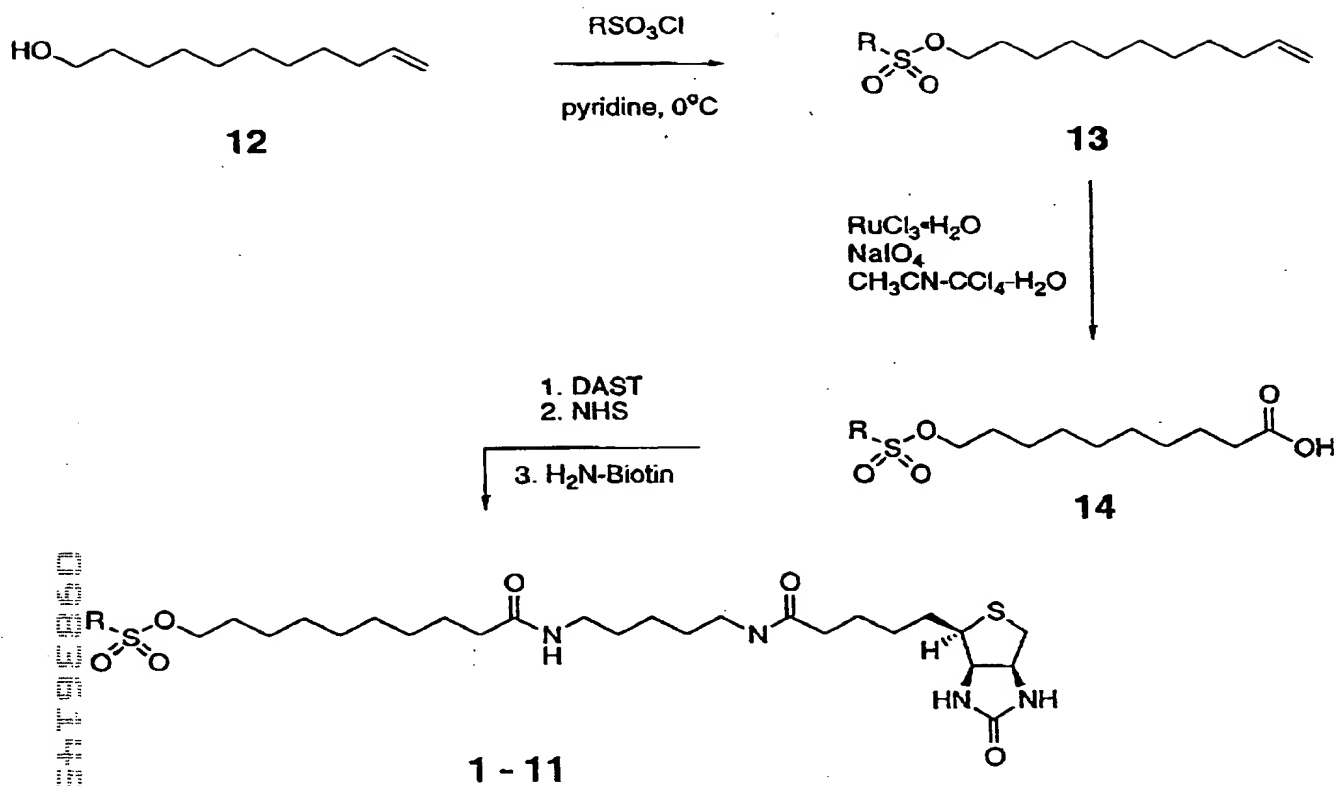


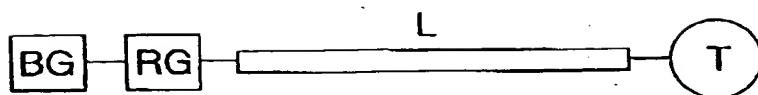
FIGURE 9



10-undecen-1-ol

FIGURE 10

A.



B.

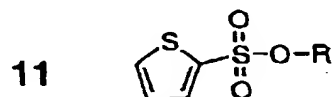
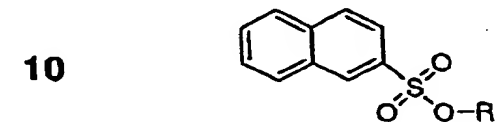
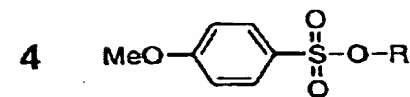
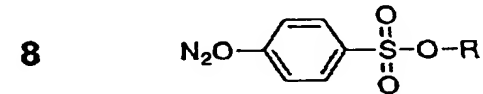
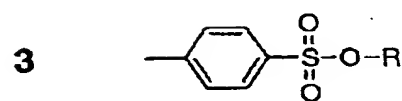
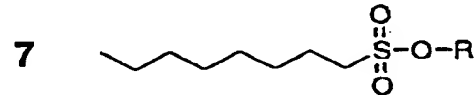
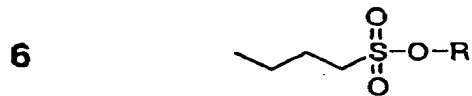
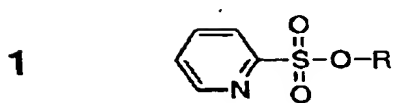
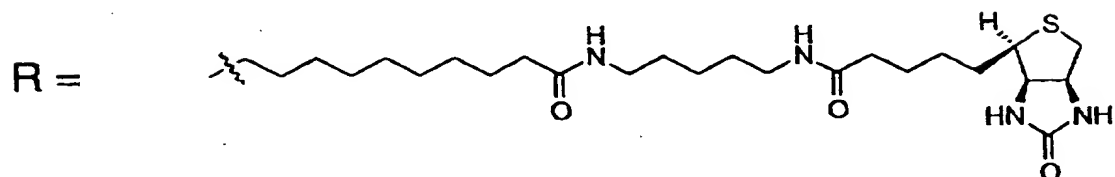
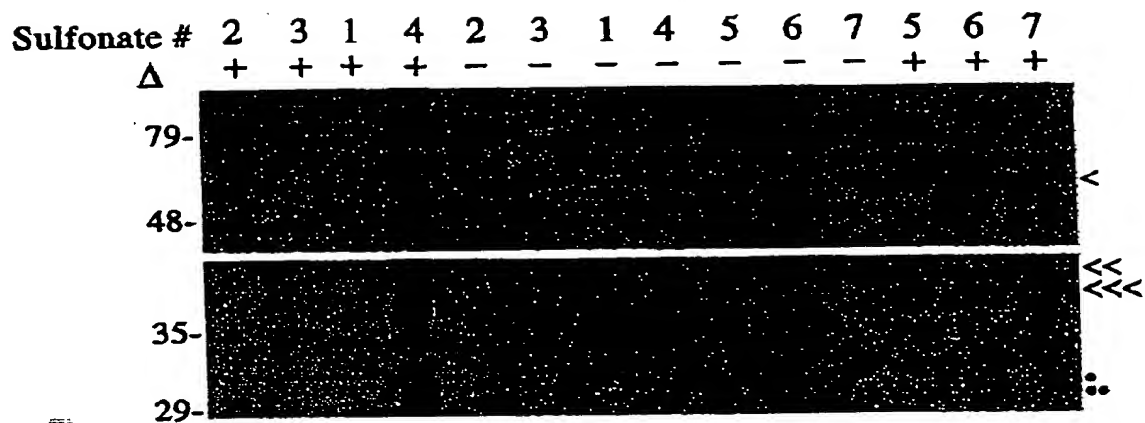
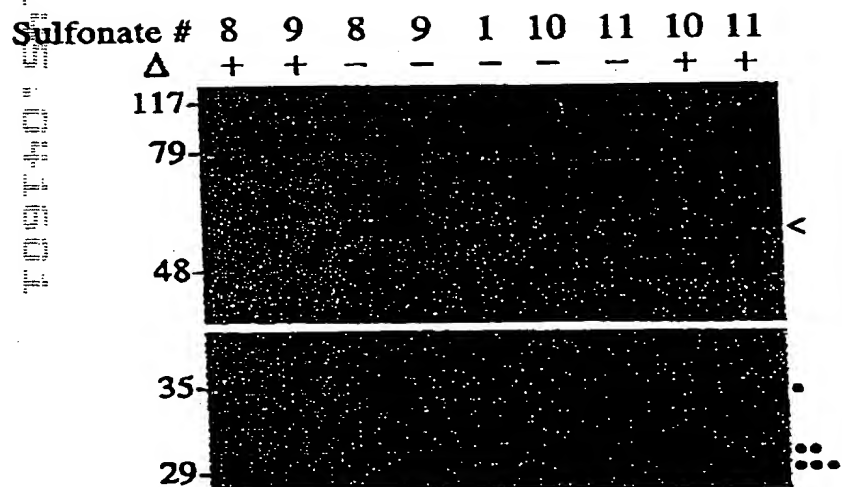


FIGURE 11

A



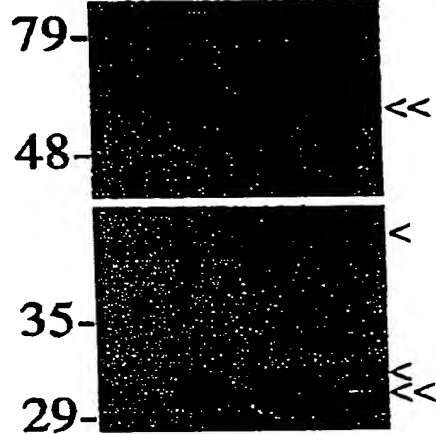
B



090361041001
T00T40"041001

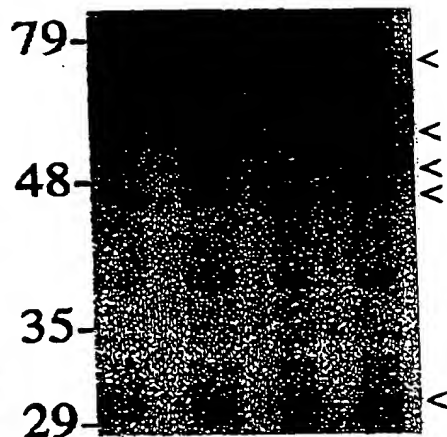
A

Sulfonate # 1 1 5 5

$$\Delta + - - +$$


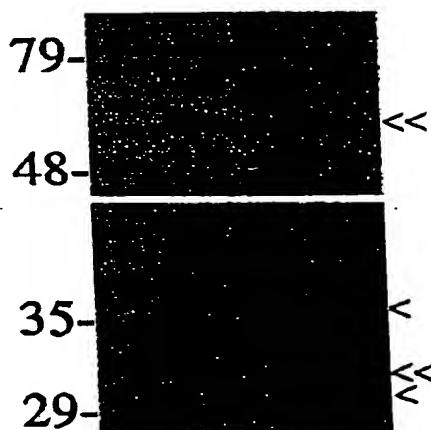
1 1 5 5

+ - - +



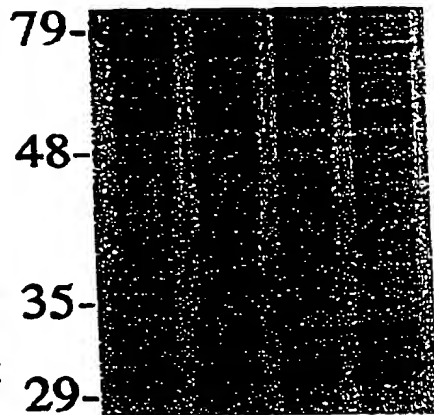
B

Sulfonate # 1 1 9 9

$$\Delta \quad + \quad - \quad - \quad +$$


1 1 9 9

+ - - +



BIG

FIGURE 13

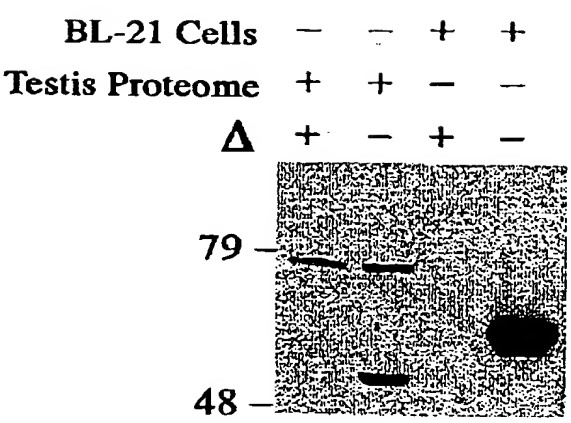
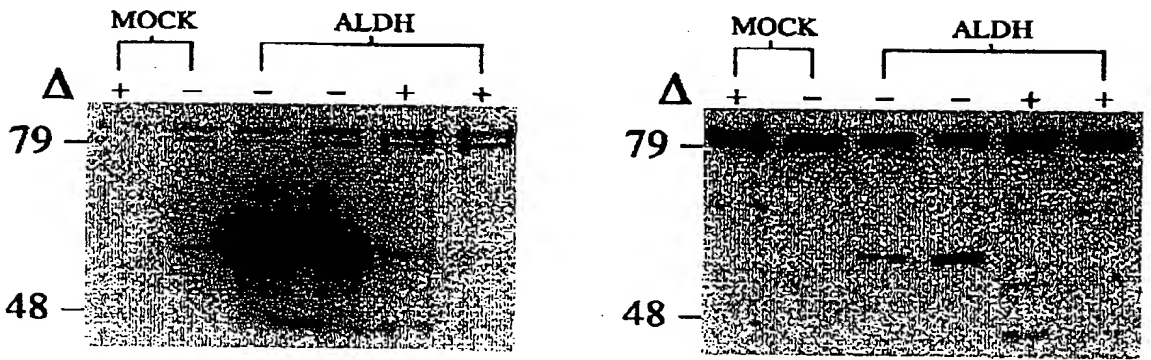
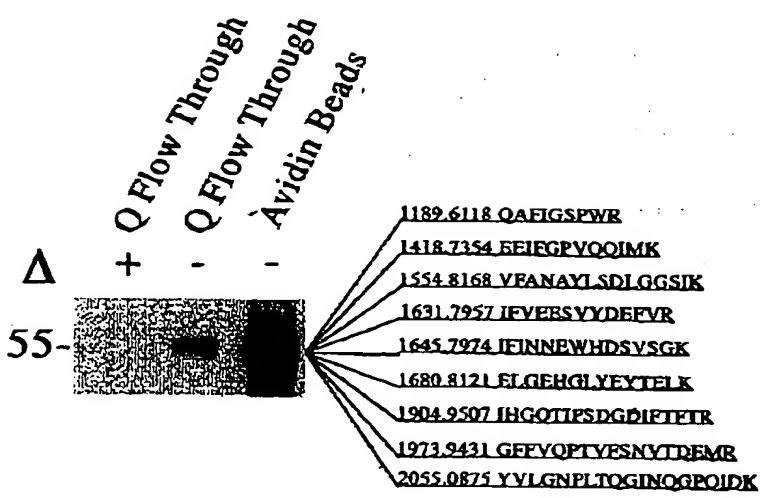
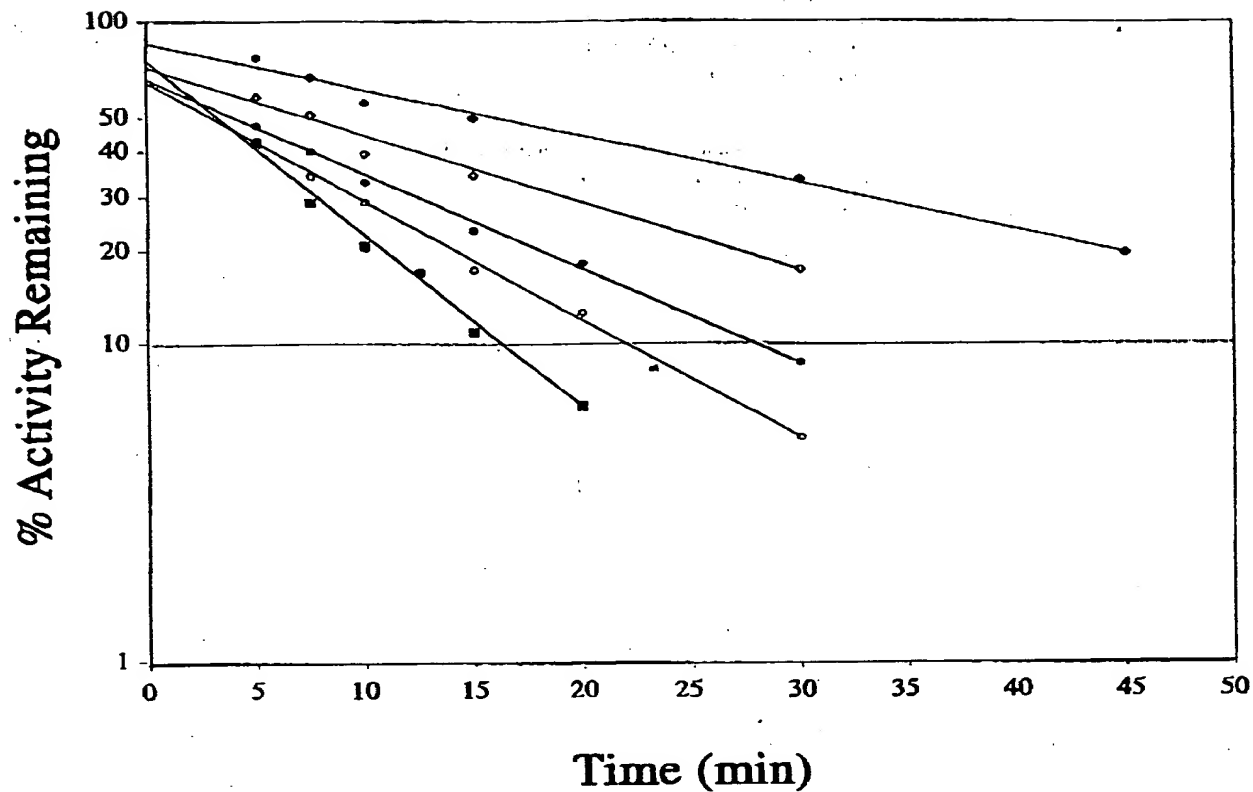


FIGURE 14

A



B

Competitor #	-	-	15	17	16	15	17	16
[Competitor (μ M)]	0	0	5	5	5	50	50	50
Δ	+	-	-	-	-	-	-	-

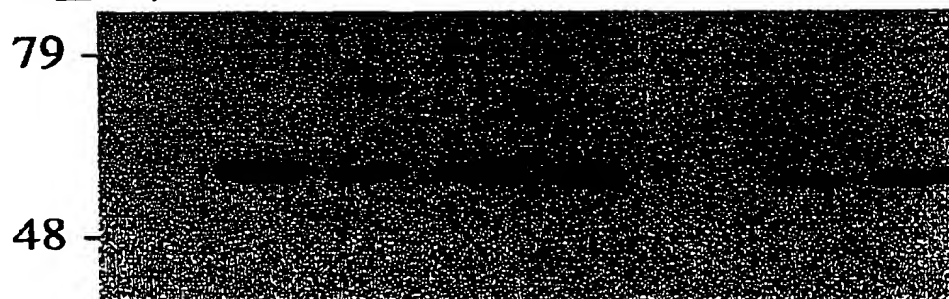


FIGURE 15

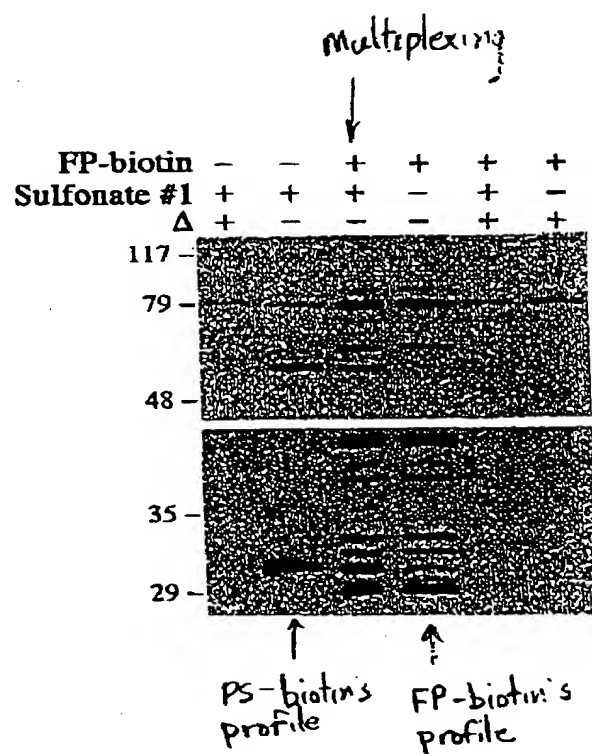
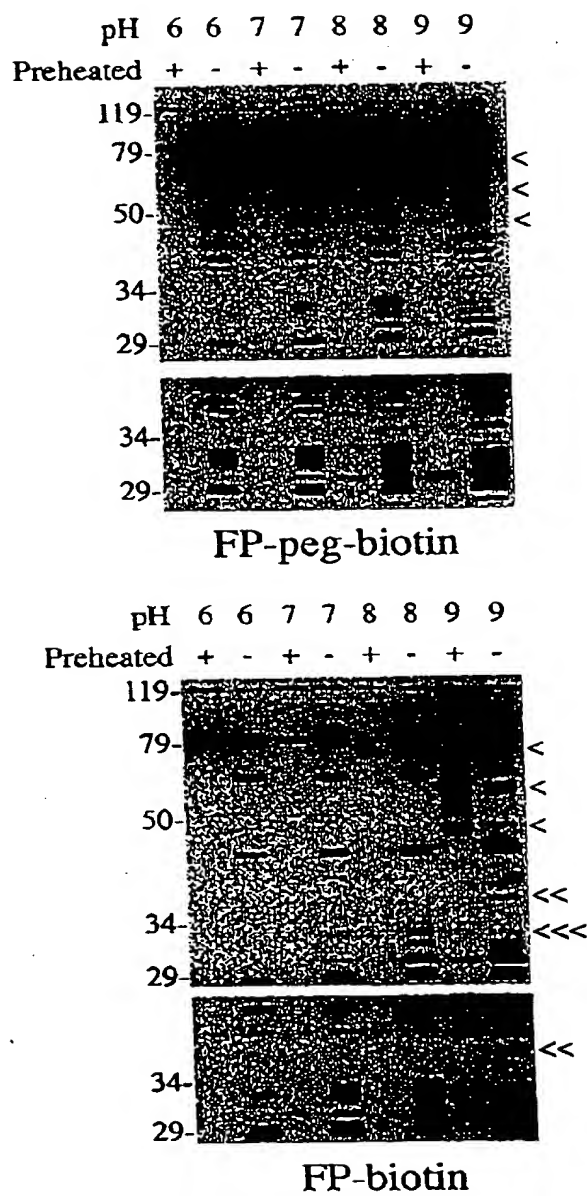


FIGURE 16



090644 044004
T00T00 044004

FIGURE 17

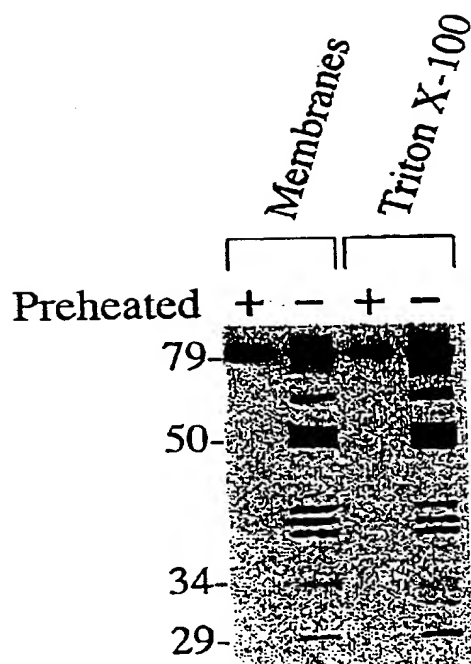
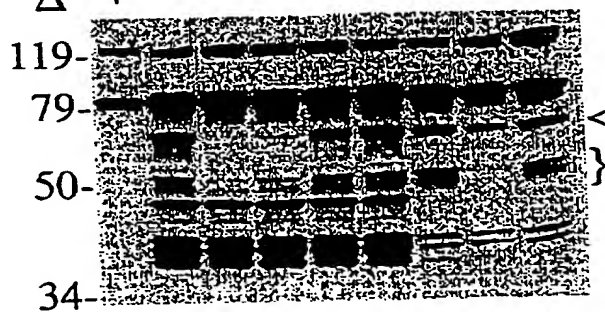


FIGURE 18

FP-peg-biotin	+	+	+	+	+	+	-	-	-
FP-biotin	-	-	-	-	-	-	+	+	+
OTFMK	0	0	200	50	5	1	0	200	50
Δ	+	-	-	-	-	-	-	-	-



109340-04100

FIGURE 19

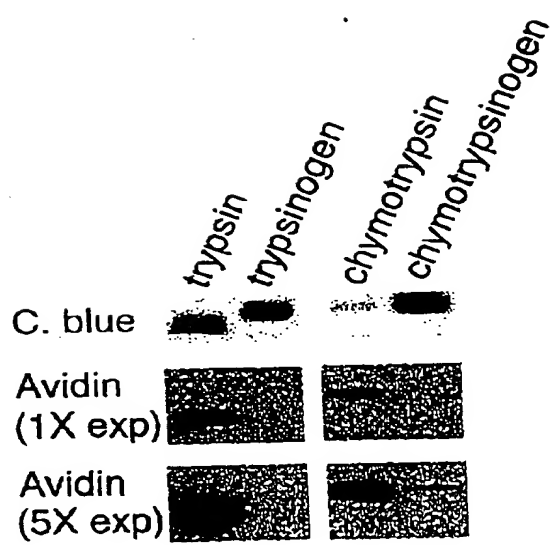
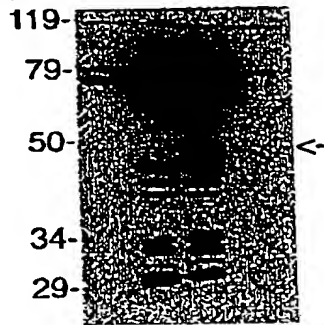


FIGURE 20

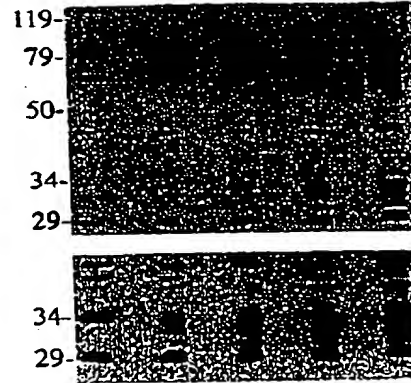
A

FP-peg-biotin	-	-	+	+
FP-biotin	+	+	-	-
Preheated	+	-	-	+



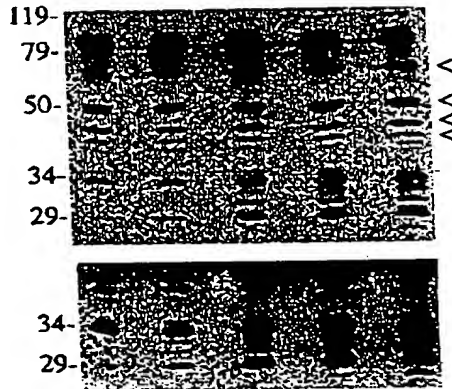
B

FP-biotin (μ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



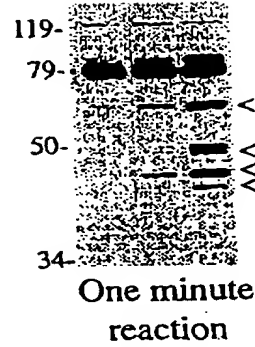
C

FP-peg-biotin (μ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



D

FP-peg-biotin (μ M)	1	2	8
--------------------------	---	---	---



One minute reaction

FIGURE 21

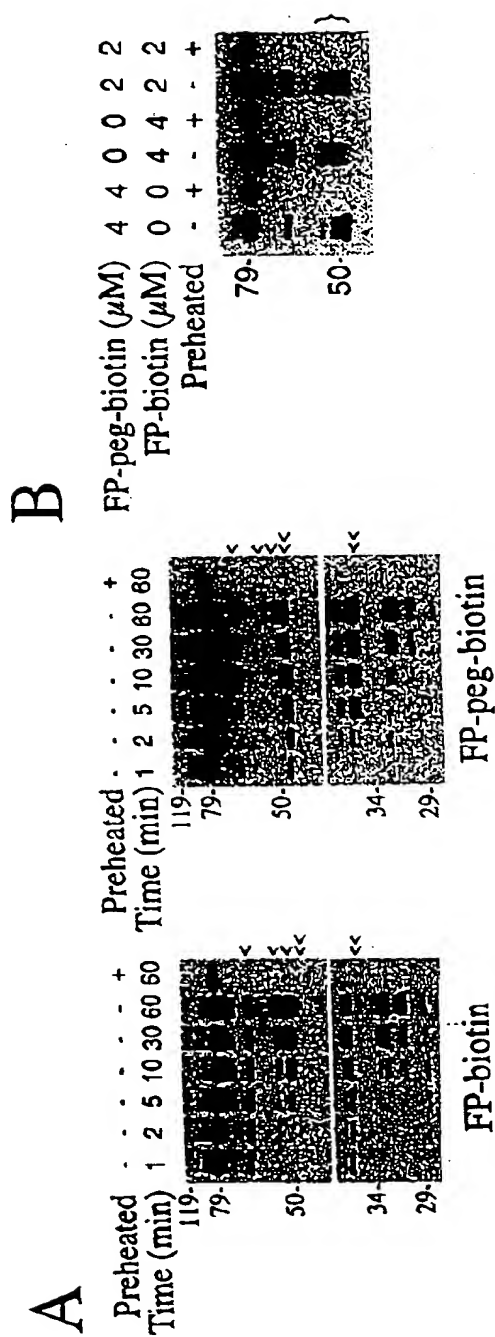


FIGURE 22

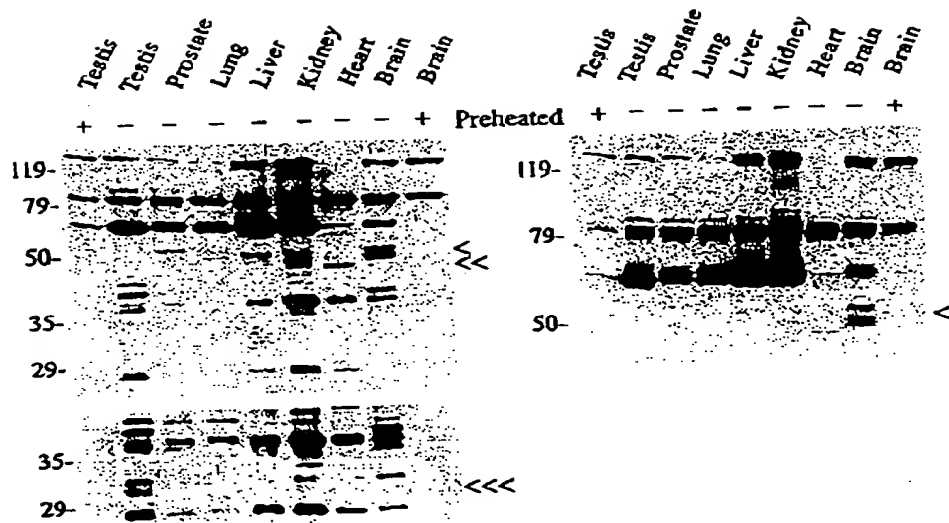


FIGURE 23

